201-14301A

Propanoic acid, 2-hydroxy-, compd. with 3-[2-(dimethylamino)ethyl] 1-(2-ethylhexyl) (4-methyl-1,3-phenylene)bis[carbamate] (1:1) CAS No. 68227-46-3

U. S. EPA HPV Challenge Program Submission

February 2003

Submitted by

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TEST PLAN
Propanoic acid, 2-hydroxy-, compd. with 3-[2-(dimethylamino)ethyl] 1-(2-ethylhexyl) (4-methyl-1,3-phenylene)bis[carbamate] (1:1)
CAS No. 68227-46-3

ENDPOINT	Information Available (Yes/No)	Testing Required (Yes/No)
Physical-chemical Data		
Melting Point	No	No
Boiling Point	No	No
Vapor Pressure	Yes*	No
Water Solubility	No	Yes
Partition Coefficient	Yes*	No
Environmental Fate and Pathway		
Photodegradation	Yes*	No
Stability in Water	Yes*	No
Transport/distribution (Fugacity)	Yes*	No
Biodegradation	No	Yes
Ecotoxicity		
Acute Toxicity to Fish	No	Yes
Acute Toxicity to Aquatic Invertebrates	No	Yes
Acute Toxicity to Aquatic Plants	No	Yes
Toxicological Data		
Acute Toxicity	No	Yes
Repeated Dose Toxicity	No	Yes**
Repro/Developmental Toxicity	No	Yes**
Genetic Toxicity *in vitro* (Gene Mutation)	No	Yes
Genetic Toxicity *in vitro* (Chromosomal Aberration)	No	Yes

*Calculated Data will be used.
**A combined repeated dose/reproductive/developmental toxicity study will be conducted.

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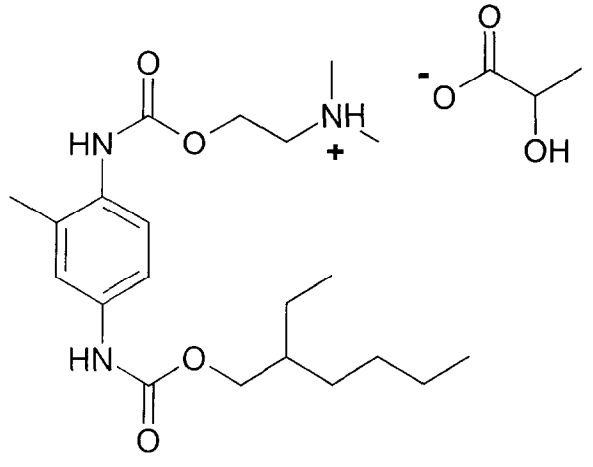
1. Sponsoring Company

PPG Industries, Inc is the manufacturer of Propanoic acid, 2-hydroxy-, compd. with 3-[2-(dimethylamino)ethyl] 1-(2-ethylhexyl) (4-methyl-1,3-phenylene)bis[carbamate] (1:1) and is the sponsor of this substance for the U.S. Environmental Protection Agency's HPV Chemical Challenge Program.

2. Test substance

Propanoic acid, 2-hydroxy-, compd. with 3-[2-(dimethylamino)ethyl] 1-(2-ethylhexyl) (4-methyl-1,3-phenylene)bis[carbamate] (1:1) is an intermediate to produce a resin that is used for the production of paint products. The majority of this material is currently used at one PPG location. The remaining small portion of this material is sold to two other companies. Its molecular structure is as follows:



The test substance is produced commercially in the presence of Methyl Isobutyl Ketone (MIBK) solvent (~5%) and then diluted with 2-butoxy ethanol (~20%) to facilitate its handling. At this concentration in this solvent system, the material is a clear, light yellow, liquid. In order to prepare an isolated sample of the test substance for HPV testing, an attempt was made to drive off the solvents by distillation. However, this removal of excess solvents from the substance resulted in the formation of polymeric by-products. It is not possible to prepare the isolated (solvent-free) test substance for HPV testing. Instead, the test substance was prepared in MIBK as usual and then diluted with water. The aqueous solution was then vacuum stripped to remove the MIBK and a portion of the water that resulted in a sample containing the test substance at 71% solids in water.

Since the test substance is an intermediate to be used for a production of resin and the vapor pressure is expected to be very low, the only potential exposure would be by skin contact to workers, not to the general public.

3. Criteria for Determining Adequacy of Data

All relevant data were reviewed and assessed for adequacy according to the standards of Klimisch *et al.* (1977). Four reliability categories, 1-reliable without restriction, 2-reliable with restriction, 3-not reliable, and 4-not assignable, have been established and a rating of 1 and 2 were considered to be adequate.

4. Test Plan

The Test Plan was developed using approaches that attempt to utilize minimum numbers of animals for testing while still meeting the data development requirements of the HPV program. A thorough data search was conducted using various available databases and company reports prior to development of the Test Plan. Additionally, consideration was given to possible use of Structure Activity Relationships or read-across comparison techniques based on a category approach. However, no relevant data were identified in either the published or unpublished literature. As detailed in the specific sections of the Test Plan below, the proposed studies incorporate the animal saving techniques recommended by EPA in their October 14, 1999 letter to HPV chemical sponsors.

4.1 Physical/Chemical Properties

No measured data are available for melting point, boiling point, vapor pressure, octanol/water partition coefficient, and water solubility. Because producing pure material (free of solvents) for the purposes of determining a melting point and a boiling point is not possible, no meaningful data can be generated. Therefore, no testing for melting and boiling points is recommended.

Data for vapor pressure and partition coefficient (Kow) are estimated (calculated) using a modeled approach. The vapor pressure is estimated to be 2.62E-8 mm Hg and the partition coefficient (Log KOW) is estimated to be 4.38. No testing for these end points is recommended.

Since no data are available, measurement of water solubility is recommended.

4.2 Environmental Fate/Pathways

Data for photodegradation, stability in water, and environmental transport were estimated using the EPIWIN/HYDROWIN/AOPWIN program. The estimated photodegradation hydroxyl radical rate constant was estimated to be 113.7966 E-12 cm^3/molecule-sec with a half-life calculated to be 1.128 hours. Aqueous base/acid-catalyzed hydrolysis indicates that the estimated total Kb for pH >8 is 1.343 E+1 L/mol-sec with a half-life calculated to be 14.339 hours. Level III fugacity modeling indicates that the test substance should partition to water (14.4 %), air (3.23E-5 %), soil (79.1 %), and sediment (6.52 %). No data on biodegradability is available. In order to fulfill this end point, a ready biodegradability study (OECD Guideline 301) is recommended.

4.3 Ecotoxicity

There were no reports or studies concerning the toxicity of the test substance to fish, aquatic invertebrates, or aquatic plants. In order to fulfill HPV toxicity testing requirements, ecotoxicity testing in fish (OECD Guideline 203), aquatic invertebrates (OECD Guideline 202), and algae (OECD Guideline 201) is recommended.

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

There were no reports or studies found that presented data on acute mammalian toxicity. In order to fulfill HPV toxicity testing requirements, one acute toxicity study (OECD Guideline 425, oral toxicity, up and down method) with a supplemental component of *in-vitro* cytotoxicity test is recommended. The cytotoxicity test could provide useful information to estimate starting doses for *in-vivo* acute toxicity testing. This testing approach minimizes the number of animals used for testing to develop the needed information.

4.4.2 Repeated Dose Mammalian Toxicity

There were no reports or studies found that presented data on repeated dose mammalian toxicity. In order to fulfill HPV toxicity testing requirements, a combined repeated dose/reproductive/developmental toxicity screening study (OECD Guideline 422) is recommended. This testing approach minimizes the number of animals used for testing to develop the needed information.

4.4.3 Genetic Toxicity

There were no reports or studies found that presented data on genetic toxicity. In order to fulfill HPV toxicity testing requirements, it is recommended to conduct two *in-vitro* genetic toxicity studies (OECD Guidelines 471 and 473).

4.4.4 Reproductive/Developmental Toxicity

There were no reports or studies found that presented data on reproductive/developmental toxicity. In order to fulfill HPV toxicity testing requirements, a combined repeated dose/reproductive/developmental toxicity screening study (OECD Guideline 422) is recommended (see section 4.4.2). This testing approach minimizes the number of animals used for testing to develop the needed information.

5. Summary

A thorough data search was conducted using various databases and company reports. However, no existing published or unpublished data on the test substance were found. Estimated information derived from commonly used models is presented to satisfy most physical/chemical properties and environmental fate data end points. Additional studies recommended are water solubility and a biodegradation tests. No data are available on ecotoxicity or mammalian toxicity. Acute ecotoxicity tests in fish, aquatic invertebrates, and algae are recommended. In order to minimize the number of animals needed to estimate the health effects end points, it is proposed that an up and down method will be used in the conduct of an acute oral toxicity study and that *in-vitro* methods are utilized for genetic toxicity. Additionally, a combined repeated dose/reproductive/developmental toxicity study (OECD Guideline 422) is recommended in order to fulfill the repeated dose, reproductive, and developmental toxicity endpoints while minimizing the number of animals required.